Proposal of Recommendations for a Personalised Precision Medicine National Strategy

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Executive Summary

According to the United States National Research Council (NRC), Precision Medicine involves the adaptation of medical treatment to the individual characteristics of each patient.

This makes it possible to identify patients who differ in regard to their susceptibility to a particular disease, their biology and/or the prognosis of the disease, or their response to a particular treatment. This identification is carried out through the analysis and integration of genomic information and information from other omic sciences, imaging techniques with clinical information and information on the patient's environment.

This makes it possible to apply preventive or therapeutic treatments in those patients who will benefit from them, avoiding potential side effects and giving patients who will not benefit from them the chance to obtain a better treatment at the most suitable time. This avoids the unnecessary expense associated with the treatment of patients who will not benefit from it.

Therefore, it represents a paradigm change in the way that healthcare is provided, incorporating more effective and safer treatment and diagnostic strategies and providing solutions to guarantee the sustainability of healthcare systems.

Nevertheless, the widespread application of Personalised Medicine poses significant challenges in regard to the application of the approximations that have proven their efficacy, effectiveness, safety and cost effectiveness. Over the last few years, countries such as the US and Japan and England, France, Finland and Germany in Europe, among many others, have been implementing strategies and plans for Personalised, Precision, or Genomic Medicine at the national level.

As the starting point of this document, we analysed the principal initiatives that have been implemented in those countries, in order to identify common elements and learn from the successful initiatives. Many of these countries are undoubtedly focusing on promoting the transformation involved in the application of Personalised, Precision, or Genomic Medicine, considering it to be a national priority, a distinguishing element in the positioning of their economies and supporting the companies involved to develop new products and services related to it.

The regulatory and legislative framework, the integration of information in Electronic Health Records, the generation and analysis of data, access to the shared information that is generated, the firm support of research and innovation projects, public-private collaboration, training of professionals who will apply it and the necessary participation of patients at all stages of the process are just a few of the many aspects to be considered when designing and developing a strategy with these characteristics. All of this in order to adequately organise and plan a transformation of our National Health System that will benefit patients and improve the sustainability of the system. This transformation is already a reality in many areas.

To facilitate the understanding of the concept and combine the nuances that different experts, professionals in the field and society in general attribute to the terms Personalised and Precision Medicine, the Roche Institute Foundation would like to promote the use of the term Personalised Precision Medicine (PPM).

In light of this analysis and with the perspective of a multidisciplinary group of experts, we propose a total of 56 recommendations in 6 areas of action, which range from regulations to R&D&I and that are aimed at providing a base for the preparation of a future and highly desirable, Personalised Precision Medicine Strategy in Spain.

Acknowledgements

Thanks to the group of experts, formed to prepare this document, for their valuable contributions, for sharing their outlook on the current situation and the desirable future scenario. Their work has made it possible to identify the aspects on which a future National Strategy of Personalised Precision Medicine should focus and reach a consensus regarding proposed recommendations for each one of them.

And also to the experts in the different fields of expertise, who, through individual interviews, contributed their views and recommendations for the application of Personalised Precision Medicine in the customary clinical practices of our National Health System.

Many thanks for their collaboration and commitment to the implementation of Personalised Precision Medicine in our National Health System.

Group of experts

Guillermo Antiñolo
Head of Service/Full Professor (HUVR/Univ. of Seville). Clinical Management Unit for Genetics, Reproduction and Foetal Medicine. Virgen del Rocío Hospital. Scientific director of the Medical Genome Project (MGP).

Juan Cruz Cigudosa
President of the Spanish Association of Human Genetics (2013-2017).Head of the Molecular Cytogenetic Group of the National Oncology Research Centre (CNIO).

Jesús García-Foncillas
Director of the Oncology Institute and Department of Oncology, Fundación Jiménez Díaz University Hospital, Autonomous University of Madrid.

María Jesús Lamas
Head of the Hospital Pharmacy Service of the University Hospital Complex of Santiago (CHUS).

Adrián Llerena
Director of the Centre for Clinical Research Infanta Cristina University Hospital, Extremadura Healthcare Service (CICAB). Professor of the Medical School of the University of Extremadura (UEX). Member of the Pharmacogenomics Working Party of the European Medicines Agency (EMA).

Carlos López Otín
Professor of Biochemistry and Molecular Biology in the Department of Biochemistry of the Medical School of the University of Oviedo. Co-director of the Spanish project in the International Consortium of Cancer Genomes.

Núria Malats
Head of the Genetic and Molecular Epidemiology group of the Human Cancer Genetics Program. National Centre for Oncology Research (CNIO).

Felipe Prósper
Director of the Cellular Therapy Area and Co-director of the Haematology and Haemotherapy Service of the University of Navarre Clinic (CUN).

Julio Sánchez Fierro
Lawyer and consultant of International Organisations. Member of the Healthcare Committee of the Congreso de los Diputados and Assistant Secretary of Healthcare. Trustee of the Roche Institute Foundation.

Ruth Vera
Head of the Medical Oncology Service of the Hospital Complex of Navarre (CHN). Vice-President of the Spanish Society of Medical Oncology (SEOM).

1. Introduction

A PRELIMINARY REFLECTION, WHAT DO WE MEAN BY PERSONALISED PRECISION MEDICINE?

As the starting point for the preparation of this document, we addressed the need to reflect on the definition of **Personalised Precision Medicine** itself. From the available literature, our initial conclusions were that there is no widely-accepted consensus as to what should be understood by Personalised Medicine or Precision Medicine, with both terms normally used interchangeably.

In the United States, the latest initiatives in this area generally use the term Precision Medicine. However, at the European level, the strategies and recommendations developed in recent years identify with the term Personalised Medicine. Several of the specialists consulted within the framework of this document were perceiving the concept of Personalised Medicine to be evolving towards the term Precision Medicine.

In 2011, the National Research Council (NRC) of the United States published the following definition:

Precision Medicine according to the National Research Council (NRC)

> *"Tailoring of medical treatment to the individual characteristics of each patient.*
>
> *It does not literally mean the creation of drugs or medical devices that are unique to a patient, but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment.*
>
> *Preventive or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not."*
>
> Source: Toward Precision Medicine. Building a Knowledge Network for Biomedical Research and New Taxonomy of Disease. National Research Council of the National Academies. 2011.

Over the course of the project, we determined that there is no single definition or a clear distinction between the concepts of Personalised Medicine and Precision Medicine, with perfectly valid reasons presented in favour of the use of each one, with slight nuances.

In response to this situation, the Roche Institute Foundation wants to promote the use of the term Personalised Precision Medicine (PPM), in its efforts to improve the understanding of the concept. This is an attempt to combine the nuances that the different experts, professionals in the field and society in general attribute to each term into a single term and in turn avoid excluding important aspects or entering into partial connotations of each one.

Personalised Precision Medicine (PMM) is understood as the identification and application of the most effective preventive, diagnostic and therapeutic approach for each patient, using Precision Medicine as a tool.

PPM represents a paradigm change in the way that healthcare is provided, incorporating more effective and safer treatment and diagnostic strategies and providing solutions to guarantee the sustainability of healthcare systems. Nevertheless, the widespread application of Personalised Medicine poses significant challenges in regard to the application of the approximations that have proven their efficacy, effectiveness, safety and cost effectiveness.

Aware of the importance and potential of its application, over the last few years, several countries have been implementing strategies and plans for Personalised, Precision, or Genomic Medicine at the national level. In many cases, these strategies have the express commitment of their respective governments, a specific budget and a financing framework that is suitable for incorporation into the healthcare system.

For years, the Roche Institute Foundation has been working intensively to generate consensus and recommendations aimed at the rational and efficient incorporation of PPM into clinical practice.

Within this framework, we have promoted the preparation of this document, in order to review the current development of Strategies of Personalised, Precision, or Genomic Medicine in the main countries in our area and propose, through the consensus of a multi-disciplinary group of experts and in line with European directives, recommendations that could serve as the foundation for a future National Strategy of Personalised Precision Medicine in Spain.

It is our hope that this work will be taken into consideration for future strategic developments that we undoubtedly consider to be vital to apply PPM in such a way as to maximise the benefit for patients and our healthcare system.

2. Objectives

WHY IS A STRATEGY FOR PERSONALISED PRECISION MEDICINE NECESSARY?

We feel that a strategy with these characteristics, which serves as a general framework for the implementation of PPM in our National Health System would make it possible:

- To contribute to improving clinical **results** in patients, with the consequent improvement in quality and quantity of life.
- **Stay ahead** of the continuous scientific advances in this area, laying out work lines, laying the groundwork for implementing them, accelerating and facilitating access and adapting them to the needs of our environment.
- Contribute to the **equality and access** to top-quality personalised precision care.
- Contribute to the **rationalisation** of healthcare costs and the **sustainability** of our National Health System.
- Put Spain on the **cutting edge** of the application of PPM.
- Advance the **generation of data** that make it possible to generalise the initiatives that demonstrate the cost effectiveness of PPM.

> The general goal of this document is to identify and spread a proposal of recommendations for the future preparation of a National Strategy for Personalised Precision Medicine, defining a reference framework at the national level for application in customary clinical practice.

The following actions were carried out to achieve these objectives:

- Initiatives for the design and implementation of Personalised, Precision, or Genomic Medicine strategies at the international level were analysed. Based on this analysis, we were able to extract the key aspects for possible application at the national level.
- Different initiatives related to Personalised, Precision, or Genomic Medicine at the national level or the level of the Regional Communities of Spain were identified an analysed. This analysis enabled us to identify work lines, resources and initiatives that a future national strategy should consider, coordinate, incorporate and promote.
- Based on the aforementioned analyses, basic common elements to be considered in the design and development of PPM at the national level were identified.
- The principal unaddressed needs and key aspects for the application of PPM in our healthcare system were identified through interviews and meetings with experts.
- Lastly, in light of the previous diagnosis, consensus recommendations were proposed for the preparation of a Strategy of Personalised Precision Medicine in Spain.

3. Work methodology

As the starting point for the project, a group of experts was formed and performed the functions of the Advisory Committee for the duration of the project. Its functions included the identification of successful national and international initiatives, issuing opinions and recommendations on different aspects and the revision and validation of the documentation generated within the framework of the project.

Experts in different areas of knowledge were also identified, in order to complement the group's viewpoint in specific areas.

As a group, the specialists provided their views in the areas of knowledge with the greatest potential and impact in the practical application of PPM strategies, including Medical Oncology, Haematology, Hospital Pharmacy, Genetics, Biochemistry and Molecular Biology, Pathological Anatomy, Epidemiology and Bio-computing, among others. Professionals with different profiles of responsibility in the field also provided their opinions, including hospital managers, persons responsible for the development of R&I policies at the Regional level, scientific directors of healthcare research institutes, representatives of patient associations, etc.

The members of the group of experts, as well as the experts interviewed, participated in the project on an individual basis.

The execution of the actions was structured into three work phases:

Phase 1: Situation diagnosis. Analysis of strategies, plans and policies regarding Personalised, Precision, or Genomic Medicine

- This phase analysed the principal experiences implemented nationally and internationally, in order to extract the key aspects that would make it possible to design and develop a Plan or Strategy for Personalised Precision Medicine in Spain.

- In addition, interviews with experts and members of the group of experts were used to identify needs, deficiencies, or areas on which the possible future Personalised Precision Medicine Strategy should focus.

Phase 2: Identification of key elements for the definition of a Personalised Precision Medicine Strategy

- During this phase, the key aspects were proposed for consideration in a Personalised Precision Medicine Strategy and the situation in Spain with respect to those aspects was analysed, reaching a consensus regarding the principal aspects in which recommendations would have to be issued to incorporate advances and improvements.

- **FIRST WORKSHOP:** After this analysis, a Workshop was held with a group of experts to agree upon the key elements in each one of the aspects that had been identified.

WORKSHOP 1

Phase 3: Consensus of a proposal of recommendation for a Personalised Precision Medicine Strategy

- **SECOND WORKSHOP:** Once a consensus was reached regarding the areas on which to issue recommendation , a workshop was organised with the goal of identifying and agreeing upon proposed recommendations for the design and development of a Personalised Precision Medicine Strategy. These recommendations were prioritise in terms of impact and feasibility.

WORKSHOP 2

Phase 4: Preparation, validation and distribution

- Lastly, this document was prepared, for the purpose of spreading the proposed recommendations that had been agreed upon for the preparation and development of a future Personalised Precision Medicine Strategy in Spain. Finally, the document was revised and validated by the group of experts.

4. Analysis of successful experiences at the international level in Personalised, Precision, or Genomic Medicine

Over the last few years, several countries have been implementing strategies and **plans for Personalised, Precision**, **or Genomic Medicine** at the national level. As the starting point, we analysed the principal initiatives that have been implemented in those countries, in order to identify common elements and successful initiatives in different countries. The analysis focused on identifying organisational models, allocated resources, collaboration and agents involved and principal actions implemented, among other aspects.

Plans and Strategies in Personalised, Precision, or Genomic Medicine

The list of Plans and Strategies that were analysed is included below.

International initiatives analysis

Country	Plan or Strategy analysed
United States	The Precision Medicine Initiative (PMI).
United States	Personalised Medicine Coalition (PMC).
United Kingdom	
England	Personalised Medicine Strategy.
Scotland	Scotland's Precision Medicine.
Germany	Personalised Medicine Action Plan.
France	France Médecine Génomique 2025.
Finland	Finland´s Genome Strategy.
Estonia	Estonian Genome Project.

General initiatives at the European level analysed

European Alliance for Personalised Medicine (EAPM).

PERMED Proyect.

The details of the principal characteristics of the initiatives analysed at the international level and of the general initiatives at the European level are included in Annex 1.

Conclusions of the analysis of initiatives at the international level

1. Several countries in our environment have been implementig **strategies and initiatives for Personalised, Precision, or Genomic Medicine at the national level**. Many of these have the **express commitment of the government, a specific budget and a financing framework** that is suitable for incorporation into the healthcare system.

2. The goal of these strategies is to foster **research and innovation** that allows the generation of new advances and mainly, their application in normal clinical practice, improving health results, establishing a framework of trust and transparency that guarantees equality and access.

3. The application of PPM in clinical practice is perceived as a **new paradigm**, which represents a **relevant change in the way in which healthcare is provided.**

4. These strategies cover the application of PPM for **prevention, diagnosis and treatment** of diseases.

5. The different strategies recognise the value of PPM to help guarantee the **sustainability** of healthcare systems.

6. The principal strategies establish a network of **public-private collaborations,** including the participation of different agents as a means of achieving their objectives.

7. The strategies all indicate, as a critical point, the generation of information on **health results,** which makes it possible to evaluate the initiatives in real conditions and the training of healthcare professionals and society.

8. Within the framework of European initiatives to promote Personalised, Precision, or Genomic Medicine, different groups are working on issuing recommendations to **harmonise policies**, introduce **quality standards** and spread best practices in regard to **ethical conditions and secure access to shared information.**

9. Several strategies include the creation of a **network of sequencing platforms or centres for Genomic Medicine** as one of their central elements. These centres are involved in the standardisation and generation of quality information, as well as in the general aspects of training or advising.

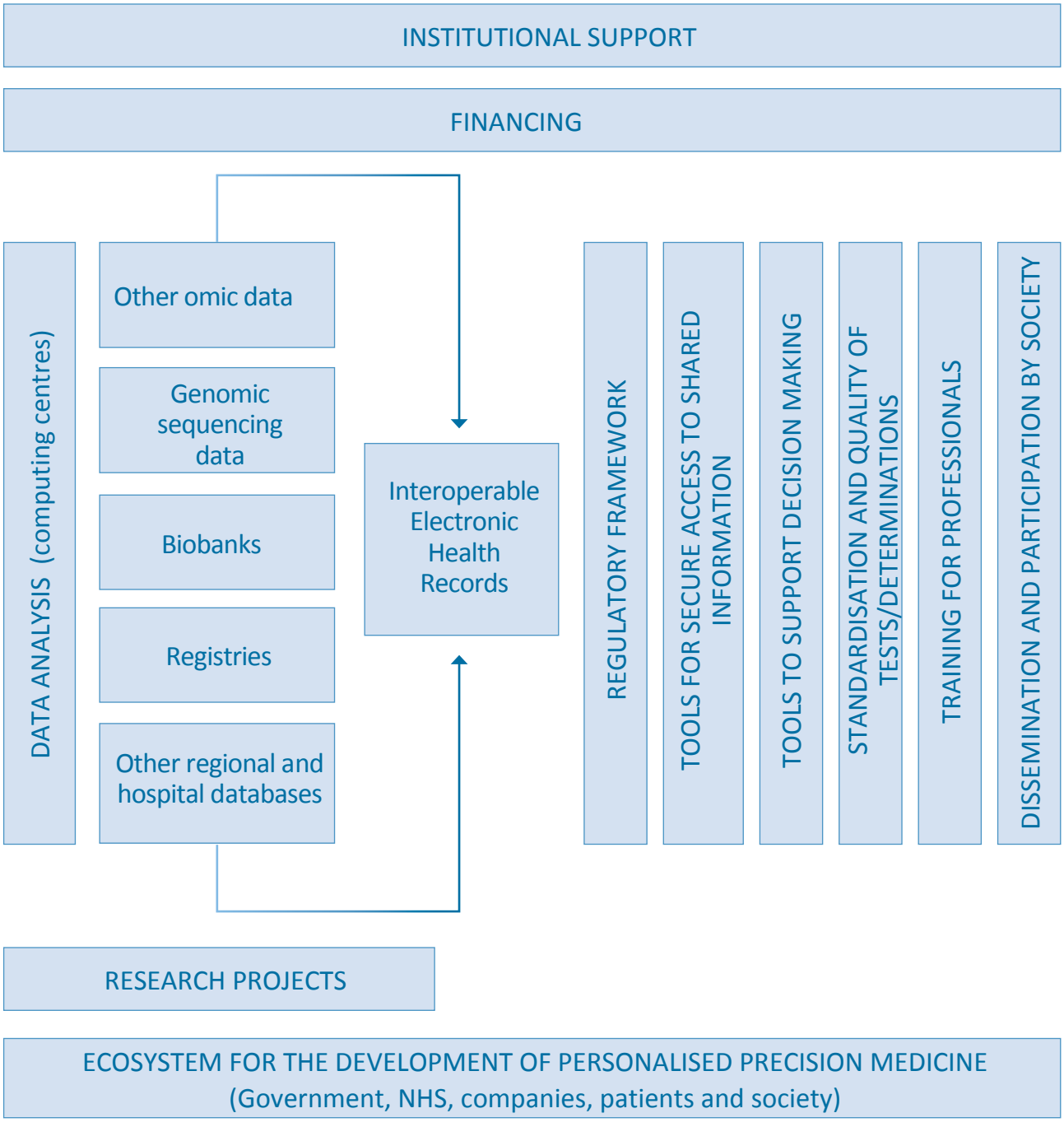
10. The **integration of the clinical information** with the data generated by different sources (omic sciences, imaging technologies, lifestyle habits and social environment), as well as the development of i**nteroperable Electronic Health Records**, are common challenges that must be faced by this type of strategies.

11. The National Computing Centres are consolidating themselves as the tool to respond to the needs related to the **storage, management and use** of the large volume of data generated.

12. Different strategies have shown the need for studies of joint co-development of **drugs and biomarkers** and **Big Data** analysis to generate new knowledge.

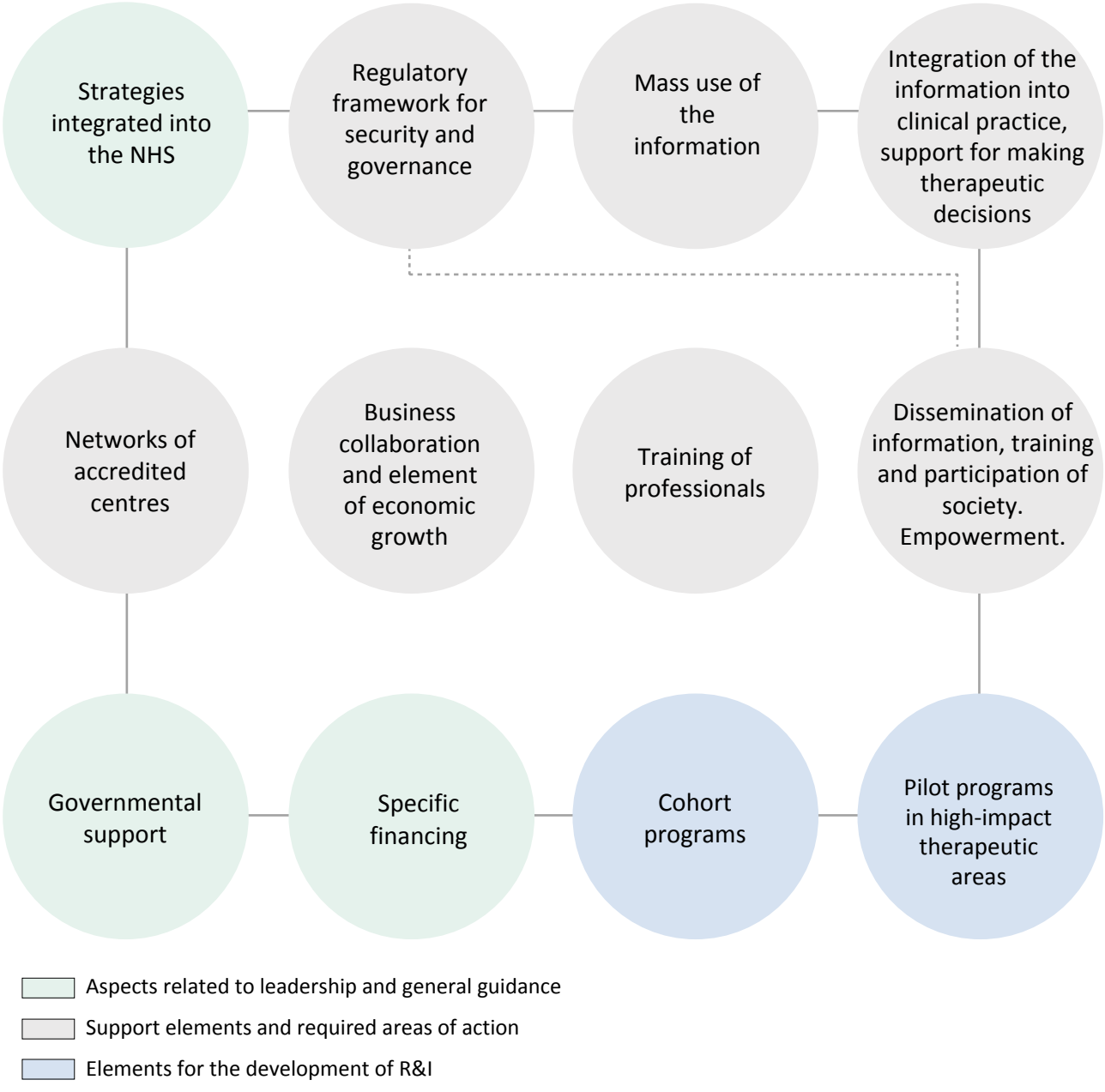
Common elements in Personalised, Precision, or Genomic Medicine strategies

The analysis of the actions carried out within the different strategies analysed, identified the following elements as **necessary** for the development of Strategies at the national level:



What aspects do the analysed strategies have in common?

Common elements identified in the National Strategies analysed.



5. Principal initiatives at the national and regional levels in Personalised, Precision, or Genomic Medicine

HOW ARE WE WORKING AT THE NATIONAL AND REGIONAL LEVELS?

Policies, strategies and initiatives for Personalised, Precision, or Genomic Medicine at the national level

Even though to date no transversal strategy for Personalised, Precision, or Genomic Medicine has been developed in Spain, there are several strategies and initiatives that develop the different aspects of its implementation at the national and regional levels.

At the national level, different National Strategies address goals and recommendations for the development of the PPM. Specifically, the most recent updates of the National Health System's Strategies for Cancer and Rare Diseases include aspects related to the application of Personalised, Precision, or Genomic Medicine in these types of diseases.

In 2013, the Carlos III Institute of Health launched the first call for **cutting-edge Projects aimed at the field of Personalised Medicine (PMP).**

Also, the different collaborative research networks (CIBER and RETICS) financed by the ISCIII and the Healthcare Research Institutes are developing projects in the area of PPM.

The development of the Integrated Plan on Genomic Medicine in Catalonia, the Medical Genome Project (MGP) in Andalusia and the Future Clinic project in the Valencia Region are some of the plans and programs that are underway at the regional level. In addition to these initiatives and other specific projects, different Regions are including specific lines of research on PPM in the frameworks of their RIS3 smart specialisation strategies.

The details of the principal initiatives at the national and regional levels in Personalised, Precision, or Genomic Medicine are provided in Annex 2.

6.Proposal of Recommendations for the preparation of a Personalised Precision Medicine Strategy in Spain

The analysis of the international strategies and recommendations identified 6 areas in which to identify needs and recommendations.

Areas for which the Proposal of Recommendations for a Personalised Precision Medicine Strategy in Spain is provided

For each one of these 6 areas, the key and common elements that need to be taken into consideratin when designing a Personalised Precision Medicine Strategy were analysed based on the experiences in the surrounding countries. Based on these, the needs and key areas of action for which a proposal of priority recommendations for the design and development of a future Personalised Precision Medicine Strategy was finally agreed upon.

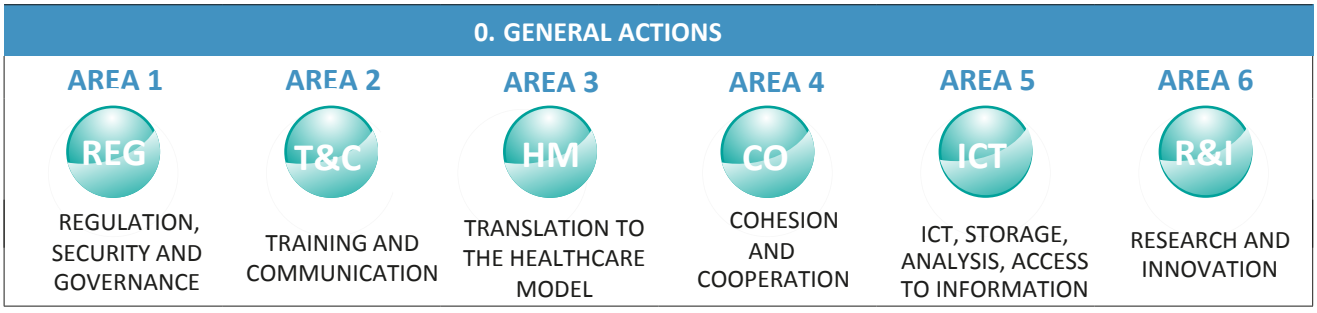
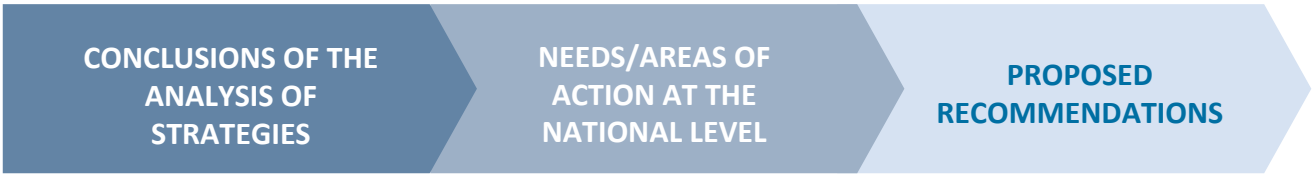


Diagram of the methodology used for the presentation of conclusions and proposal of recommendations



All Personalised Precision Medicine Strategies should consider the patient as the central axis and promote the involvement of all of the agents in the sector in the development of the strategy, from the professionals of the National Health System and researchers, experts and opinion leaders in different areas of knowledge, to the industries in the healthcare sector.

The main objective of the strategy should be to identify action that make it possible to transfer Personalised Precision Medicine to clinical practice, in an orderly manner that guarantees quality, equality and the sustainability of our Healthcare System.

GENERAL ACTIONS

Conclusions of the Analysis of Strategies	Key areas	Needs/areas of action at the national level
• The application of PPM in clinical practice is perceived as a new paradigm, which represents a relevant change in the way in which healthcare is provided. • Several countries, aware of this reality, have been implementing strategies and plans for Personalised, Precision, or Genomic Medicine at the national level. Many of these have the express commitment of the government, a specific budget and define an adequate financing framework, making it possible to develop the tools needed to implement PPM, in accordance with pre-established standards. • The goal of these strategies is to foster research and innovation that allows the generation of new advances and mainly, their application in normal clinical practice, improving health results. To do this, they establish a framework of trust and transparency and equal access conditions, as well as indicators to measure progress in implementation and results of the proposed actions. • These strategies cover the application of PPM to prevention, diagnosis and treatment of diseases. • The different strategies recognise the value of PPM to help guarantee the sustainability of healthcare systems. • Within the framework of European initiatives to promote Personalised, Precision, or Genomic Medicine, different groups are working on issuing recommendations to harmonise policies, introduce quality standards and spread best practices in regard to ethical conditions and secure access to shared information.	Common framework of action Leadership	• Need for a general coordination framework, which organises and promotes the incorporation of PPM into the NHS and the initiatives developed at the regional level. • Leadership of the Ministry of Health, Social Services and Equality and the Carlos III Institute of Health (ISCIII) needed.

General **Proposal of Recommendations**

1. Prepare a National Strategy by common agreement that serves as a general framework for the development of Personalised Precision Medicine in our NHS, aimed at facilitating application in clinical practice, with an appropriate regulatory framework, in an equitable manner, guaranteeing quality, efficiency and compliance with ethical standards, contributing to the sustainability of the system and promoting research and innovation.
2. Allocate a specific budget to this National Strategy.
3. Frame governance and debate on the definition and development of the Strategy in the Interterritorial Board, with the support of the MSSSI. Involve the MINECO, MECD and the ISCIII in its development.
4. Promote coordination of the actions included in the National Strategy for Personalised Precision Medicine and the rest of the national strategies in the area of different pathologies and with a future national e-health strategy.
5. Foster the role of the ISCIII in the development of actions to promote research, innovation and training in PPM and the support of the Spanish Agency for Medication and Healthcare Products (AEMPS) in the execution of the Strategy.
6. Identify successful initiatives implemented in other countries and analyse the problems detected and the results generated by the implementation.

AREA 1: REGULATION, SAFETY AND GOVERNANCE

Conclusions of the Analysis of Strategies	Key areas	Needs/areas of action at the national level
• Development of an ad hoc regulatory framework for the development of the strategies. • Incorporation of opinions of patients and representatives from society in the development of the regulatory framework, policies and ethical aspects related to the use of molecular information. • Creation of Scientific Committees to provide guidance for the development of the strategies. • Creation of groups with experts in specific areas to design and execute specific actions included in the strategies.	Generate trust Transparency Participation	• Development of a regulatory framework and a framework for action that generates trust and promotes transparency among professionals, patients and society in general. • Development of the existing legislative framework, especially for application to genetic counselling and diagnosis and the use of biobanks in the area of healthcare. • Involvement of scientific societies, companies and representatives of society in the aspects of regulation, security and governance.

Proposal of Recommendations AREA 1
on REGULATION, SAFETY AND GOVERNANCE

1. Develop the regulatory frameworks that organise and provide cohesion to the system to evaluate new drugs, biomarkers and diagnostic methods associated with PPM and their incorporation into the NHS, with the involvement of the AEMPS and the Spanish Network of Agencies for Evaluation of Healthcare Technologies and Services of the National System.

2. Develop the aspects of the regulatory framework that guarantee privacy and make it possible to use the information generated (pseudo-anonymization or reversible anonymization).

3. Develop the Biomedical Research Act and Bio-bank Act, in regard to the aspects related to the area of care.

4. Promote the application of the European Parliament and Council Regulation, regarding the protection of personal information and the free circulation of information, at the national level, in the aspects that affect the implementation of PPM in the area of care.

5. Develop directives for the application of the Personal Information Protection Act to the handling of patient information related to the application of PPM, that transmit confidence in regard to the handling of the information in relation to both care and research.

6. Involve representatives of scientific societies, companies and society in general in the development of the aforementioned regulations, along with specialists in medical law.

7. Disseminate the applicable regulatory framework (described in recommendations 1-4) among professionals, patient associations and society.

AREA 2: TRAINING AND COMMUNICATION

Conclusions of the Analysis of Strategies	Key areas	Needs/areas of action at the national level
• Promotion of specific education beginning in schools and especially after graduate training, to build a society with the knowledge to understand ad participate in the application of scientific progress. • Support of the acquisition of new personal skills and abilities, through the incorporation of specific content in graduate training, specialised healthcare training and post-graduate training. • In regard to the training at the graduate level, updating courses of study, in health science departments, to include content on PPM. • In terms of ongoing medical education, incorporation or strengthening of content on PPM in existing programs. • Organisation of collaborative forums for dissemination of information and debate onn implications and actions to further PPM. • Organisation of events at the regional level, with participation by physicians, pharmacists and opinion leaders to increase awareness of PPM. • Publication of true and accurate information, freely accessible through websites and social networks. • Actions aimed at guaranteeing that professionals and patients receive sufficient information to face the ethical problems deriving from the use of molecular information.	Education in PPM in graduate studies New specialisations integrated into the NHS Ongoing training Empowerment patients and society	• Reinforcement of the content needed to apply PPM in Courses of Study at the graduate level. • Improved training and specialisation of professionals in areas that require the confluence of knowledge from different specialisations. • Improvement of general training in Clinical Genetics. • Reinforcement of the training of specialists in genetic counselling. • Official recognition of the bio-computing specialisation. • Empowerment of society. Improve society's level of understanding in regard to the implications, possibilities and advantages of PPM. • Generation of trust in society through information, participation and transparency.

Proposal of Recommendations AREA 2
on TRAINING AND COMMUNICATION

1. Reinforce the genetic, pharmacogenetic and pharmacogenomic content and content from other omic sciences in Courses of Study of health sciences degrees.

2. Increase the offering of post-graduate and master's programs specialised in PPM, with a multi-discipline focus.

3. Develop areas of training in genetics/genomics in different specialisations.

4. Reinforce contents on genetic counselling and regulatory aspects in the specialised training plans. Develop the clinical aspects of the Clinical Genetics specialisation.

5. Promote the involvement of the principal scientific societies in the development of the post-graduate and ongoing training offerings in PPM.

6. Promote the organisation of forums and the publication of content in freely-accessible mediums that make it possible to publicise the concept of PPM and increase society's awareness of it.

7. Increase the training offerings aimed at journalists and specialised Health informers, involving professional associations in the development process.

8. Promote the official certification of specialists in bioinformatics, ensuring stable incorporation of these professionals into the National Health System.

9. Promote hybrid training paths that facilitate the acquisition of knowledge of different specialisations or emerging specialisations.

AREA 2: TRANSFER TO THE HEALTHCARE MODEL

Conclusions of the Analysis of Strategies	Key areas	Needs/areas of action at the national level
Access and financing: • Establishment of criteria for the validation of biomarkers and the clinical value of encountered mutations, for use in clinical practice. • Creation of observatories and carrying out studies for the development and application of value assessment models, including economic assessment (cost-benefit) of new biomarkers and tests. • Definition of alternative financing models for the incorporation of new services based on PPM. • Creation of observatories to track the evolution of the field of PPM (including scientific, medical, technological and international regulation aspects). • Incorporation of patient perception of the results obtained in the entire process of evaluating value, approval and financing. • Preparation of an Investment plan and budget planning. **Quality and standardisation** • Standardisation. Development of consensus and recommendations so that sequencing, tests and other determinations are carried out following standardised quality procedures, reducing variability and facilitating the generation of valid and comparable data. Development and implementation of a quality assurance system, with the involvement of scientific societies. • Development of sequencing platform networks and/or genomic medicine centres, as a central element of the strategies. These centres are involved in both the standardisation as well as the generation of high-quality information, as well as in training and counselling actions. **Generation and access to information based on evidence for decision making:** • The strategies all indicate the generation of information on results on health as a critical point, allowing the initiatives to be evaluated under real conditions. • Periodic updating of guidelines, protocols and other tools to support decision making, based on evidence to ensure that they include best practices. **Patient counselling:** • Development of systems to provide patients with information on possible consequences of the analysis and handling of molecular information.	Evaluation Financing Quality and Standardisation Guidelines and Protocols Patient counselling	• Guarantee orderly execution of tests and determinations, equal access to results and quality reports. • Improve access and use of information in Electronic Health Records, for the development of studies on results on health and economic assessment. • Improve and adapt the process for the evaluation of healthcare technologies and clinically relevant biomarkers, incorporating the criteria of economic evaluation. • Guarantee equitable access to innovations. • Guarantee financing of validated options and the sustainability of the system. • Improve training and guarantee adequate time to provide specific counselling to patients.

Proposal of Recommendations AREA 3
on TRANSFER TO THE HEALTHCARE MODEL

1. Promote the certification of centres that are references of scientific and technological excellence, to carry out highly complex determinations and sequencing, contributing to the development of validated and reproducible methodologies.

2. Ensure compatibility between different information systems to use and analyse the recorded information to evaluate the health results obtained, direct and indirect costs, develop cost-effectiveness studies.

3. Define the mechanisms that allow better communication and coordination between the agencies responsible for the evaluation of drugs and healthcare technologies.

4. Adapt the system for the evaluation of innovations to be incorporated into the service portfolio that includes criteria of effectiveness, clinical validity and utility and economic criteria.

5. Develop financing systems based on value and health results.

6. Update and implement guidelines and protocols for the application of biomarkers, diagnostics and genetic counselling based on best practices and available evidence.

7. Formalise genetic counselling consultations, promoting adequate dimensioning and planning.

8. Define adequate tools and processes to inform patients regarding possible consequences of improper use of information, the possibility of incidental discoveries, etc., based on best practices and available evidence.

9. Promote the development of pilot experiences in specific areas or with specific pathologies to test the suitability of the care model and the proposed actions (throughout the process, from evaluation and approval and validation, to patient information) for generalisation in the healthcare system.

10. Foster participation of Primary Care in the implementation of PPM initiatives and especially in the development of personalised prevention programs.

AREA 4: COHESION AND COOPERATION

Conclusions of the Analysis of Strategies	Key areas	Needs/areas of action at the national level
• Development of Offices to coordinate the strategies at the national level. These offices oversee the development of interoperability standards, compliance with privacy requirements and secure exchange of data between systems. In the case of the US, it provides a single point of contact for the coordination of data, biological samples, patient information and development of research studies. • Providing incentives for shared use of information. • Development of structures and procedures to access large volumes of shared information, for Big Data analysis. • Development of user-friendly, universally-accepted processes for gathering and sharing information. • Development of common informed consent forms that facilitate coordination between institutions. • Development of mechanisms for patient participation in the definition of tools and levels of access to their information. • The strategies analysed establish a network of public-private collaborations, including the participation of different agents as a means of achieving their objectives. • Definition of the ecosystem of entities to promote, develop and provide initiatives for Personalised, Precision, or Genomic Medicine, including the public and private sectors. • Involvement of scientific societies and patient associations in different actions of the strategies.	Shared information Ecosystem Public-private	• Creation of structures and processes that facilitate access to shared information. • Establishment of systems of pseudo-anonymization or reversible anonymization, that guarantee protection of data and the right to privacy. • Identification of minimum common clauses in informed consent forms that facilitate optimum use of the information. • Definition of the role and promotion of the involvement of scientific societies in the development of the Personalised Precision Medicine Strategy. • Development of a stable framework for collaboration with the private sector, in a win-win model and contribution to the sustainability of the system.

Proposal of Recommendations AREA 4
on COHESION AND COOPERATION

1. Define the framework for the coordination of the Strategy, which should be defined and developed by the Interterritorial Board.

2. Define the mechanisms and allocate financing to structures that enable the sharing of the information generated by multiple institutions, including actions through the Carlos III Institute of Health.

3. Promote the incorporation of common clauses in the different existing informed consent forms.

4. Facilitate and promote the involvement of scientific societies in the development of the strategy. Request their collaboration specifically on the development of the regulatory framework, system for evaluating the value contribution of innovations to be incorporated into the NHS, training of specialists, development of structures for access to shared information and dissemination of activities.

5. Foster the involvement of patient associations that are transversal and highly representative. Development of their role in patient empowerment, the development of the regulatory framework and access to information, as well as in the definition of clauses in informed consent forms.

6. Implement innovative public procurement (IPP) initiatives and research, development and innovation projects in public-private collaboration

AREA 5: STORAGE, ANALYSIS and ACCESS TO INFORMATION

Conclusions of the Analysis of Strategies	Key areas	Needs/areas of action at the national level
• Development of tools that facilitate the generation and access to information by clinics, facilitating its use in clinical practice and updating based on the scientific advances that take place. • Development of collections systems that can be integrated to allow work to be done jointly. • Integration of clinical information with the data generated by different sources (omic sciences, imaging technologies, life-style habits and social environment), as well as the development of interoperable health records, are common challenges facing the strategies analysed. • Improvement of simple use systems, integrated with different resources, for example from biobanks. • Development of systems to allow clinics to visualise analyses and data display interface for the patient. • Development of solutions for the storage of large volumes of information. • The National Computing Centres are consolidating themselves as the tool to respond to the needs related to the storage, management and use of the large volume of data generated. • Development of solutions for Big Data analysis and processing. Development of artificial intelligence and predictive analytical tools. • Development of tools for the analysis of scenarios and in silico analysis to guide new research developments and the generation of algorithms for application in clinical decision making.	Electronic Health Record Storage and Analysis	• Identification of the minimum data set to be collected. • Advances in harmonisation and interoperability of health records. • Improvement of the structure and system for using information. • Organise and optimise the use of computing resources, management, analysis and storage of data.

Proposal of Recommendations AREA 5
on STORAGE, ANALYSIS AND ACCESS TO INFORMATION

1. Promote the implementation of tools that enable the integration of clinical data, pharmacogenomic data and information from other omic technologies, imaging technologies, lifestyle information, prior adverse effects, etc. in the Electronic Health Record (Population Health Management).

2. Promote the harmonisation of Electronic Health Records (EHR), allowing the use of data of interest.

3. Promote the development and implementation of data mining, which allows the use of the available relevant information, both structured and unstructured.

4. Provide infrastructure and resources for computing, handling, analysis and storage of data. Identification of centralised infrastructure and service nodes that allow access to useful shared information.

5. Optimise existing resources and promote the establishment of collaboration agreements with existing specialised centres of reference.

AREA 6: RESEARCH AND INNOVATION (R&I)

Conclusions of the Analysis of Strategies	Key areas	Needs/areas of action at the national level
• The principal strategies identify leaders in specific areas who participate in the governance of the strategies through committees or leading pilot programs in specific areas. • Public-private research consortiums are defined. • Collaboration networks are established at the national level and strategic alliances and consortiums for the development of projects at the international level. • Development of mass genomic analysis studies in the population and generation of patient cohorts. • Reinforcement of biobanks that facilitate specialised support. • Development of platforms for omic sciences (genomics, proteomics, metabolomics, transcryptomics, epigenomics, pharmacogenomics, etc.) and medical imaging. • Changes in the process of developing new medications: identification of the sub-populations that are of the greatest interest, through biomarkers, from the initial phases of drug development. • Development of basket trials (clinical trials based on genetic mutations, instead of affected tissue/ organ).	Leadership Networks Cohorts Studies focused on mutation Co-development in initial phases	• Co-development in initial phases. • Involve the principal cooperative networked research structures in the development of the strategy. • Allocation of stable financing for the development of strategic projects. • Generation well-phenotyped healthy population information. • Promote independent clinical research for the co-development of biomarkers, identification of sub-populations and basket trials. • Promote trials aimed at generating data in patient sub-populations. • Promote lines of innovation in PPM in public-private collaboration.

Proposal of Recommendations AREA 6
on RESEARCH AND INNOVATION (R&I)

1. Identify leaders in specific areas of PPM to lead initiatives and act as scientific references.
2. Promote the work in networks through cooperative research structures.
3. Provide financing for projects with broad scope and relevance and evaluation of results under real usage conditions. Prioritise financing of projects on PPM.
4. Strengthen the role of the biobank network in the development of the Strategy.
5. Promote the creation of public-private consortiums to promote research and innovation.
6. Promote the use and shared access to relevant data on sub-populations, generated within the framework of clinical trials.
7. Promote the development of independent clinical trials with a biomarker/drug co-development approach.
8. Promote studies to characterise variability in the healthy population (healthy phenotype).
9. Promote research that improves knowledge of the gene-environment interaction, the interaction between drugs and integration studies with omic data.
10. Promote independent studies focused on mutations, instead of the affected organ.
11. Promote studies that facilitate the application of PPM in the design of prevention strategies.
12. Promote the development of innovation projects in the area of PPM (development of diagnostic technologies/kits, new biomarkers, etc.).

ACRONYMS

AEMPS: Spanish Agency for Drugs and Healthcare Products.

CSA: Coordination & Support Action (Coordination and Support Actions in European Framework Programs and Horizon 2020).

EHR: Electronic Health Record.

GMC: Genomic Medicine Centre. NHS England.

ISCIII: Carlos III Institute of Health.

MSSSI: Ministry of Health, Social Services and Equality.

MINECO : Ministry of Economy, Industry and Competitiveness.

MECD: Ministry of Education, Culture and Sports.

PPM: Personalised Precision Medicine.

NHS: National Health Service of the United Kingdom.

PMI: Precision Medicine Initiative of the United States.

NHS: National Health System.

ICT: Information and Communication Technologies.

Annex 1. Details of successful experiences at the international level in Personalised, Precision, or Genomic Medicine

United States.

The Precision Medicine Initiative (PMI)

On 20 January 2015, President Obama announced the launch of the Precision Medicine Initiative (PMI) in the United States with the goal of developing care that is individualised to patients thanks to advances in research, technology and policies. The total budget for this initiative for the 2016 tax year was 215 million dollars.

> *"Doctors have always recognised that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals.*
>
> *You can match a blood transfusion to a blood type — that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard?*
>
> *What if figuring out the right dose of medicine was as simple as taking our temperature?"*
>
> *Barack Obama, 2015*

The initiative includes two key elements:

1. **Oncology:** Its initial focus will be the genomic study of cancer to implement more precise treatment and prevention strategies. This part of the program will be managed by the National Cancer Institute (NCI/ NIH).

2. **Cohort Program:** The goal of this program is to create a cohort of individuals for research that will reach one million participants in 2019. A multitude of biomedical data will be collected and shared, on behaviour and lifestyle, which allow to research on a wide range of diseases, both common and rare, improve knowledge of the situation in healthy individuals and detect associations between genes-environment and analyse results on health. In order to ensure constant, reflexive and opportune revision of potential problems deriving from the cohort program, an Institutional Review Board has been created, made up of experts in bio-computing, epidemiology, genomics and environmental health

With a special focus on oncology and a budget of 215 million dollars in 2016, the Precision Medicine Initiative of the United States proposed the goal of genereting a cohort of one million people by the end of 2019.

- **Recruiting of participants:** Patient recruitment was organised directly, so that any person residing in the United States could be a volunteer in the cohort either at their own initiative or through organisations.

- **Participation of citizens in the cohort:** The activities related to communication are organised and managed by a central entity. A commitment was established to allow all participants access to their own results and the aggregate results of all of the studies in which they participate.

- **Considerations on the collected data:** The initial set of patient data is collected and stored centrally. The initiative has a national Coordination Office for the development of interoperability standards and privacy requirements that allow the secure exchange of data. A pilot data collection program was developed, for the purpose of defining and testing innovative methods and technologies that make it possible to compile robust and easy-to-use data and a pilot data access program that allows participants to access their Electronic Health Record and monitor and manage their information.

- **Biobanking:** The samples gathered for the cohort will be sent to a central bio-bank, located in the Mayo Clinic, for processing, storage, recovery and biochemical analysis and/or sending to laboratories.

- **Policy Considerations and Governance:** A reference framework was developed to respond to aspects of patient consent and privacy, improper use of the information, security and exchange of data and samples. A security framework based on the Cybersecurity Framework of the National Institute for Standards and Technology is being implemented.

United States.

Personalized Medicine Coalition (PMC)

The **Personalised Medicine Coalition (PMC)**, is an independent academic organisation that is aimed at generating opinion and positioning regarding aspects that affect Personalised Medicine. **Created in 2004, it is currently made up of more than 250 institutions, including academic organisations, patient organisations, health insurance companies, computing firms, pharmaceutical companies, diagnostic companies and biotech companies, among others.**

Some of its actions include the dissemination of information on its benefits aimed at administrations, industry and the academic world and to serve as a forum to identify and publicise possible barriers or facilitators of the development of Personalised Medicine.

PMC considers education and guidance to be key priorities.

- Training of healthcare personnel and patients regarding the potential of Personalised Medicine to improve health results and reduce costs.
- Information aimed at administrations regarding the potential of Precision Medicine to improve efficacy and the efficiency of the healthcare system.
- Promotion of public policies that stimulate investment on personalised care focuses.

The Personalised Medicine Coalition (PMC) considers one of the key aspects to be providing information on the potential of Personalised Medicine to improve health results and reduce costs, aimed at healthcare professionals and patients.

The working group on PMC healthcare has published a guide for the integration of Personalised Medicine into healthcare systems, with the key points covered below:

Guide for the adoption of Personalised Medicine. PMC's Healthcare Working Group

1 Educate stakeholders

- Develop and publish the necessary information on Personalised Medicine free of charge.
- Organise collaborative forums to reach consensus on definitions and denominations.
- Promote the updating of education and training programs in medical and pharmacy schools to include Personalised Medicine.
- Incorporate Personalised Medicine into ongoing education programs for medical professionals.
- Organise regional events with physicians, pharmacists and opinion leaders to increase awareness of Personalised Medicine.

2 Empower patients

- Include patient representatives in the development of policies and practices related to the use of molecular information.
- Include persons of different ethnic groups, races, ages and genders in the clinical trials for Personalised Medicine.
- Provide advice and other support services to patients before, during and after facing ethical dilemmas related to molecular information.
- Incorporate the patient viewpoint into the decision-making processes.

3 Demonstrate value

- Organise forums with payers, suppliers and the bio-pharmaceutical and diagnostic industry, to debate processes for the evaluation of healthcare technologies and the requirements to finance them.
- Design clinical trials to serve multiple objectives, including regulatory approvals and demonstration of clinical utility.
- Develop a universally accepted process for the collection of data and shared access to results and treatments.
- Prioritise cost-benefit studies of Personalised Medicine products and services.

4 Manage clinical information

- Provide an incentive for generating shared data.
- Improve communication between the different programs to help physicians to incorporate molecular information into the making of clinical decisions.
- Include molecular information and clinical reports, as well as prior failed treatments and contraindications in the Electronic Health Records.

5 Ensure access

- Identify strategies to facilitate financing of new technologies.
- Facilitate appropriate coverage and payment policies for Personalised Medicine services and analyses.
- Incorporate principles of Personalised Medicine into alternative payment and provision models.
- Update clinical guides and tools to support the making of decisions that ensure the implementation of best practices in Personalised Medicine.

Source: Daryl Pritchard and Christopher Wells. Beyond the promise: A clinical adoption "Road Map". Personalised Medicine in brief. Vol.7, Fall 2016

United Kingdom

The 100.000 Genomes Project

The 100,000 Genomes Project

The 100,000 Genome Project was announced in December 2012 by UK Prime Minister David Cameron. It aims to sequence 100,000 genomes of National Health Service (NHS) patients and integrate the information generated with clinical data to develop personalised therapies for cancer and rare diseases.

England.

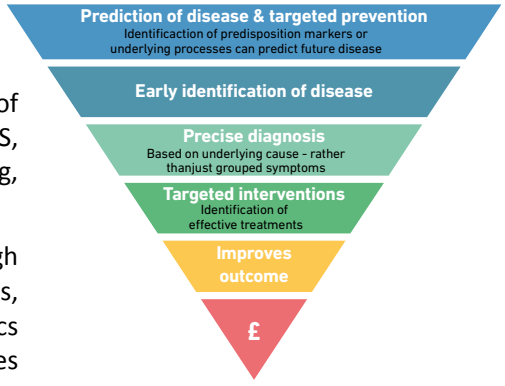
Personalised Medicine Strategy

The general objective of this strategy is to integrate Personalised and Genomic Medicine into day-to-day healthcare. To achieve this goal, in July 2015, a Personalised Medicine Strategy Board was formed, with representatives from most of the Directorates of the National Health Service (NHS).

The strategy is backed by the commitment of internal and external stakeholders and prominent experts (academics, physicians, industry, patients and the general public), including professionals who work in the field of information and analytical solutions.

The Strategy has a **National Medical Director** who plays a leadership role, which is key for the development of the Strategy.

The proposed work program has 4 critical and interdependent elements:

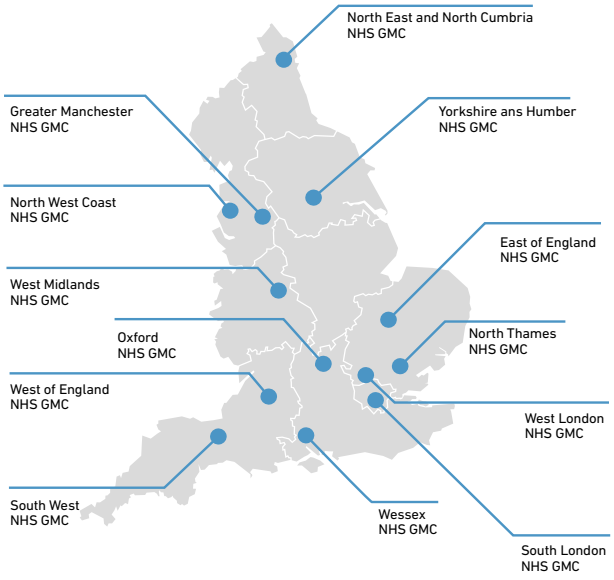


1. **BUILDING AN INFRAESTRUCTURE**: The construction of infrastructure to underpin Personalised Medicine into the NHS, inclusive of informatics and data systems, commissioning, procurement and financial frameworks.
2. **DEVELOPING A CLINICAL CHANGE MODEL**, incorporating: High impact commissioning challenges; changes to clinical pathways, pharmacogenomics and synergies bewteen companion diagnostics and medicines optimisation, but also, link the 100,000 Genomes Project's findings and NHS transformation outcomes.
3. **EMBRACING TECHNOLOGY AND INNOVATION AND CREATING THE KNOWLEDGE BASE:** Include the scientific and technological advances in all genomics and in other underpinning diagnostics: bringing in the knowledge from NHS England Digital Health Services and the National Information Board (NIB): growing artificial intelligence and machine learning applications; and an NHS England solution to the requirement for an integrated genomic and personalised medicine knowledge base with complex analytical solutions to inform both clinical practice and research and development.
4. **POLICY AND SYSTEM ALIGNMENT INCLUDING:** the *Five Year Forward View;* Department of Health and system partners inclusive of Health Education England, National Institute for Health and Care Excellence (NICE) and the Medicines and Healthcare Products Regulatory Agency (MHRA) and Healthcare Products Regulatory Agency (MHRA).

The initiatives currently underway include the 100,000 Genomes Project, the goal of which is to sequence genomes of 100,000 patients with rare diseases and common cancers in the NHS. The genome sequencing data will be integrated with the data generated from different health records.

A network of 11 Genomic Medicine Centres (GMCs) of the NHS has been defined, covering the existing network of genetic services of the NHS, including more than 200 geneticists, as well as the existing laboratories. Each GMC covers a population of between 3 and 5 million and is involved in different training, counselling and awareness actions.

NHS Genomic Medicine Centres



Source: Personalised Medicine Strategy. BOARD PAPER - NHS ENGLAND. https://www.england.nhs.uk/wp-content/uploads/2015/09/item5-board-29-09-15.pdf

Scotland.

Scotland's Precision Medicine.

Scotland's Precision Medicine Strategy is developed by two large infrastructure elements, the Scottish Genomes Partnership (SGP) and the Stratified Medicine Scotland Innovation Centre (SMS-IC).

A fund has also been created to act as a catalyst of the genome industry and develop an ecosystem for Precision Medicine in Scotland.

SCOTTISH GENOMES PARTNERSHIP (SGP). With an investment of 15 million pounds in genome sequencing technology at the Universities of Edinburgh and Glasgow and made up of 4 hospitals: Aberdeen, Dundee, Edinburgh and Glasgow.
The inclusion of the first patients from the NHS in Scotland was planned for the summer of 2016.

STRATIFIED MEDICINE SCOTLAND INNOVATION CENTRE (SMS-IC). Objectives include the integration of health records with genome sequencing information and transfer of research and innovation results to services or products that the NHS and other health systems may use. The Centre will initially offer genome sequencing to patients with critical diseases such as lung cancer.

Approximately 300 patients with rare diseases and their families will be invited to participate in the SGP project. The genome sequences and data will contribute 100,000 genomes from England and Northern Ireland to the project.

Four projects have currently been launched (for ovarian cancer, oesophagus cancer, rheumatoid arthritis and inflammatory bowel disease and chronic obstructive pulmonary disease) this make it possible to demonstrate the basic capabilities, advance quickly in the understanding of chronic diseases and design more effective treatments.

GENOMIC MEDICINE INDUSTRIAL CATALYST FUND. The objective is to facilitate collaboration, development and validation of technologies in the area of Precision Medicine in Scotland. The fund is aimed at Scottish PYMEs and international biotech companies, including the consortiums formed with academic partners who wish to form part of the Precision Medicine activities of Scotland's national program. Projects must have a defined market need and be commercially viable.

ESTABLISHMENT OF A SCOTTISH PRECISION MEDICINE ECOSYSTEM. It will coordinate resources aimed at Precision Medicine and its opportunities, integrating the results of individual research projects and improving shared access to the generated information. It will play a support role in the development of two national programs:

- **Precision-Panc:** aimed at the selection of the most suitable treatment in patients with pancreatic cancer.
- **FutureMS:** aimed at predicting the start of relapsing-remitting multiple sclerosis at the genetic level and severity in individual patients, making it possible to choose the most suitable treatments.

Source: http://www.scottish-enterprise.com/services/develop-new-products-and-services/genomic-medicine-industrial-catalyst-fund/overview; http://www.stratmed.co.uk/about-sms/; http://www.aridhia.com/use-cases/precision-medicine/precision-medicine-ecosystem/

Germany.

Personalised Medicine Action Plan

The Personalised Medicine Action Plan was introduced in February 2013 and addressed needs in three areas:

DEVELOPMENT OF SPECIFIC HEALTHCARE RESOURCES. Broader and more sophisticated diagnostics are required, with specific equipment, implementation of new therapeutic procedures, development of computer systems and properly trained healthcare professionals.

RELATION WITH THE INDUSTRY AND OTHER AGENTS IN THE SECTOR. Need to work in association with pharmaceutical and biotech companies and other industrial sectors, as well as with academic and research centres. The need to establish international research projects with a broad scope that make it possible to achieve the objectives of Personalised Medicine research.

COMMUNICATION. The need to establish an ongoing dialogue between scientists, physicians, lawyers, professionals from different social sciences and society in general, that helps generate a reference framework for the application of Personalised Medicine. Ethical, legal and social aspects must be taken into consideration, as well as communication platforms, which include interactive online resources, debate and information forums and training of specialists.

The Action Plan set the following short-term goals for the first 5 years of development.

- Faster and more precise diagnosis on the basis of validated biomarkers.
- Improved treatments thanks to closer linking of diagnosis with therapy and and the integration of data into research and medical practice.
- Increased investment in Personalised Medicine by the health care industry.
- Better public understanding of Personalised Medicine.

The German Personalised Medicine Action Plan addresses the need to develop healthcare resources, to generate strategic agreements with different agents and implement communication and training actions that are aimed at those involved in their development.

The following will be necessary to achieve these objectives:

- Validate innovative molecular biomarkers with regard to their potential for Personalised Medicine.
- Carry out pre-clinical research and phase I and II clinical trials to develop indication-specific therapeutic and preventive personalised medicine approaches.
- Evaluate clinical benefit with regard to the improvement of care.

Source: Personalised Medicine- Action Plan. Febrero 2013. http://gesundheitsforschung-bmbf.de/_media/Action_Plan_IndiMed_englisch.pdf

France.

France Médecine Génomique 2025

The French Genomic Medicine Plan was published in 2016, with a time horizon of 2025. The ethical dimension is a core part of the Plan, considering it necessary to integrate aspects related to patients, the healthcare system, research, training and the national economy into the plan. The applied model is based on shared access to data collected at the national level.

Its objectives include carrying out approximately 235,000 complete genome sequencings per year, corresponding to 20,000 patients with rare diseases and their families (approximately 60,000 genomes) and 50,000 patients with metastatic or refractory cancer (approximately 175,000 genomes).

Three goals were set for the Plan for 2025:

1. Position France among the leading countries in the application of Personalised Precision Medicine, with the capacity to export know-how.
2. Prepare for the integration of Genomic Medicine for the handling of common pathologies.
3. Establish a national Genomic Medicine industry that generates innovations in different areas: from the generation, storage and processing of mass health data for medical devices.

Positioning France as a leading country in the generation of new knowledge and strengthening France's Genomic Medicine industry were included among the goals of the French plan.

The development of the Plan considers 14 measures:

1. Deployment of a network of 12 sequencing platforms, covering the entire territory of France by 2020.
2. Establishment of a National Intensive Computing Centre ("CAD" Data collector Analyser), capable of process and manage a considerable volume of generated data and offering the first services to healthcare professionals.
3. Generalisation of Electronic Health Record (EHR), standardised and interoperable, which is indispensable for integration and use of genomic and clinical data.
4. In 2016, establishment of pilot projects for cancer, rare diseases and common diseases, for the purpose of eliminating technological, clinical and legal obstacles.
5. Preparation of a regulatory development framework based on best practices and legal and ethical standards, in order to comply with ethical requirements for the collection, storage and processing of clinical and genomic data.
6. Creation of an entity to evaluate and validate new instructions in genomic diagnostics that makes it possible to ensure the development of the existing instructions and their progressive integration into healthcare.
7. Creation of a leading technological centre for innovation and transfer, connected to the national platforms aimed at sequencing, the national intensive computing centre and the industry.

8. Definition of a business model that guarantees integration of this tool into the healthcare system in regard to health insurance and definition of the costs and conditions of reimbursement of "Genomic Medicine".

9. Promotion of public/private collaboration initiatives.

10. Specific training in universities and schools to begin building a multi and inter-discipline sector in genomic health and acquire new personal abilities and skills.

11. Definition of an adapted governing entity that allows the execution of the plan and the development of a specific monitoring and tracking tool.

12. Implementation of an observatory to track the evolution in the field of Genomic Medicine, integrating all of the medical and technological aspects and all of the international regulations.

13. Creation of an economic observatory that supports the foundations of a research program on medical-economic aspects.

14. Organisation of information and access to it, as well as participation by society's agents.

Source: France Médecine Génomique 2025. http://www.gouvernement.fr/sites/default/files/document/document/2016/06/22.06.2016_remise_du_rapport_dyves_levy_-_france_medecine_genomique_2025.pdf

Finland.

Finland´s Genome Strategy

Finland's Genome Strategy defines 7 main objectives and proposes 20 measures to achieve them, including a roadmap, which will be constantly monitored.

The measures are aimed at achieving the goal of using genome data effectively in healthcare assistance and in the promotion of health and well-being by 2020. The strategy has a budget of 50 million euros.

Objectives of Finland's Genome Strategy

Enabling goals of the Genome Strategy

1	Use of genomic data is governed by ethical principles and legislation.
2	Genomics research is closely integrated into health care.
3	Healthcare personnel have skills to use genomic data.
4	Information systems enable effective use of genomic data.

Ultimate goals of the Genome Strategy

1	Genomic data are widely used in healthcare based on individual and population needs.
2	Individuals are able to make use of genomic data in their own lives.
3	Finland is an attractive research and business environment in genomics.

The functions of the National Genome Centre in regard to the national strategy, include:

- Supervise the development of the Genome Strategy.
- Serve as a single point of contact for research stakeholders, marketing services and contracts.
- Develop a national reference database.
- Standardise and rationalise the ethical evaluation of research projects.
- Promote the creation of collaboration networks.
- Collaborate with different agents in the sector.
- Facilitate Finland's participation in international projects and evaluate the validity and utility of genetic tests at the national level.

The National Genome Centre is a central element in the development of Finland's strategy.

Source: Health through the use of genomic data. Finland´s Genome Strategy Working Group Proposal. https://www.julkari.fi/bitstream/handle/10024/126940/URN_ISBN_978-952-00-3598-3.pdf?sequence=1

Estonia.

Estonian Genome Project.

In 2014, an action plan was approved by the country's healthcare insurance fund to include Personalised Medicine approximations in prevention, which emphasises the need for adequate financing models and research into health results, including the impact of risk predictions at the genetic level on psychology and behaviour.

In 2014, the new government included the action plan to develop Personalised Medicine, based on cutting-edge genetic technology, in its coalition agreement.

In 2013, Estonia's Prime Minister recognised Personalised Medicine, as an appropriate strategy to respond to the increased load owing to non-communicable diseases, with an emphasis on prevention rather than on treatment.

In 2014, an action plan was approved by the country's healthcare insurance fund to include Personalised Medicine approximations in prevention, emphasizing the need for adequate financing models and research into health results, including the impact of risk predictions at the genetic level on psychology and behaviour.

> Estonia stands out as one of the first countries to set up population biobanks for the use of biomarkers in combination with information from health records and lifestyle habits.

Six key elements were identified to implement Genomic Medicine on a national scale:

1. Research to generate solid knowledge of the principal risk factors.
2. Electronic Health Record.
3. Automated systems to support decision making. The reports on disease risk and drug response will be included in the EHR.
4. Key professionals with specific training to use the data in daily practice and if the pilot phase is successful, it will be replicated for the rest of the population.
5. Powerful biobanks: Together with Iceland, Estonia was one of the first countries to design population biobanks for the use of biomarkers in combination with information from health records and lifestyle habits to study the most common diseases and to develop treatments.
6. Necessary infrastructure to promote secure exchange of information. Estonia has national infrastructure called the X-Road Platform. Since 2010, the medical information from hospitals, primary care and medical prescriptions has been accessible through this platform.

GENERAL INITIATIVES AT THE EUROPEAN LEVEL

In addition to the strategies and initiatives developed by the different European countries, in recent years, several institutions and consortiums have been working to identify the joint lines of work and general recommendations for their application in the different countries, contributing to the construction of common policies and the alignment of Personalised, Precision, or Genomic Medicine strategies at the European level.

Europe.

European Alliance for Personalised Medicine (EAPM)

European Alliance for Personalised Medicine

The European Alliance for Personalised Medicine (EAPM) brings together European healthcare and patient representatives who are experts in chronic diseases.

- Improve patient care, accelerating the development, access and trust in personalised care, including treatment and diagnosis.
- Promote the development of case studies, organisation of workshops, education, training and communication.

The results are recommendations for the design of policies that make it possible to use the potential of Personalised Medicine as much as possible.

Six working groups have been defined for the definition of objectives and recommendations in the following areas:

Big Data	Education of healthcare professionals	Translational research	Regulatory Matters	Access and value of innovation	Smart-Outreach

Partners	
Medical organisations / academies / policies	European Society of Cardiology, Cancer Research UK, ERS, Karolinska Institutet, ESMO
Patient organizations	EBC, European Association of Urology, European Cancer Patient Coalition, EURORDIS, EPF
Universities	Queen's University Belfast, Maastricht University, Università degli Studi di Milano
Associations	eahp, European Society of Cardiology, GIRP, hope, PGEU GPUE, ASPHER
Payers	AIM
Industry	Roche, Lilly, Pfizer, MERCK, Genomic Health, SAP, Bayer
Observers	European Commission Research & Innovation, European Medicines Agency, European Commission Health and food safety, European Commission Communications Networks, Content & Technology

Europe.

PERMED Project

This is a Coordination & Support Action (CSA) that was financed by the the 7th Framework Programme of the European Commission[1] in order to deliver a Strategic Research and Innovation Agenda (SRIA).

Consortium made up of 27 partners, which includes representatives from key agents in decision making. The aim is to develop recommendations to foster the implementation of PM in relation to research funding, the present and future potential of health systems, and, most importantly, the benefit that can accrue to the citizen.

As a result of the consortium, 5 challenges were defined, which generated 35 recommendations.

CHALLENGE 1	**Developing Awareness and Empowerment**
CHALLENGE 2	Integrating **Big Data and ICT Solutions**
CHALLENGE 3	**Translating** Basic to Clinical Research and Beyond
CHALLENGE 4	Bringing **Innovation to the Market**
CHALLENGE 5	**Shaping Sustainable Healthcare**

1. The Framework Programs constitute the principal EC initiative to promote and support R&D&I in the European Union, with the principal objective of improving competitiveness through financing mainly of research activities, technological development, demonstration and innovation under a system of transnational collaboration between companies and research institutions belonging to other countries of the European Union and Associated States, as well as third-party countries. The 7th Framework Program covered the period from 2007 to 2013.

Annex 2. Detail of principal initiatives at the national and regional levels in Personalised, Precision, or Genomic Medicine

Important initiatives and projects at the national level, or with Spanish participation at the institutional level

Initiatives and projects	Description
Network of Excellence for Research and Innovation in Exosomes http://rediex.org/	**The Rediex Network was created to promote Personalised Medicine in Spain by fomenting scientific collaboration** Rediex is an initiative financed by the Ministry of Economy and Competitiveness (MINECO), which will make it possible to advance in the development of Personalised Medicine in Spain. The network will be aimed at developing new therapeutic strategies in cancer and parasitic diseases. It will develop and unify methodologies and will accelerate the identification and development of non-invasive biomarkers and alternative control strategies for this type of disease.
Elixir https://www.elixir-europe.org/	**ELIXIR is the largest life-science data infrastructure in Europe. Its purpose is to manage, use and disseminate the large amount of information that is generated today by biomedical research.** ELIXIR is a decentralised infrastructure managed as a special project of the European Molecular Biology Laboratory (EMBL) and organised in the form of a central device to share a data network (Hub) and distributed nodes, which operates and manages in the broadest sense of the word, an interrelated collection of biological data resources and scientific tools. The Carlos III Institute of Health (ISCIII), represents Spain in ELIXIR and coordinates Spain's scientific institutions integrated into the National Bio-computing Institute (INB), which acts as Spain's scientific node. Several Spanish centres also participate in the initiative: National Centre for Oncology Research (CNIO), Genomic Regulation Centre (CRG), including the National Centre for Genome Analysis, the Pompeu Fabra University, the Biomedical Research Institute of Barcelona (IRB) and the Barcelona Supercomputing Centre. Participation in this alliance will reinforce collaboration with European groups and contribute to projects with broad scopes and importance, related to the genomics of human diseases.
Chronic Lymphocytic Leukaemia Genome Project http://www.icgc.org http://cancergenome.nih.gov)	The creation of an international consortium to study the cancer genome (International Cancer Genome Consortium, ICGC) came out of the idea of coordinating efforts and sharing knowledge to advance more rapidly and effectively[2]. The consortium's main objective is to create a complete catalogue of genetic alterations of the 50 most common cancers in the world's population. **Spain was one of the initial 8 founding countries of the consortium with the chronic lymphocytic leukaemia (CLL) Genome Project.** The consortium is committed to making all of the generated data accessible to be used freely by the scientific community, with the idea of accelerating possible application in clinical practice in the form of new diagnostic tools and the development of new drugs. The consortium also addresses all of the implications associated with the project, which includes responding to new bioethical challenges that arise, definition of clinical and pathological criteria for inclusion of patients in trials, evaluation of new technologies, development of bio-computing tools to analyse and evaluate findings and the search for methodologies to store and expeditiously use the enormous quantity of information that will be accumulated.

2 The International Cancer Genome Consortium. International network of cancer genome projects. Nature. 2010 Apr 15;464(7291):993-8. doi: 10.1038/nature08987.

Initiatives at the Regional level

Catalonia.

Integrated Genomic Medicine Plan

In December 2015, the Department of Healthcare of the Generalitat de Cataluña defined three objectives in the area of Genomic Medicine:

1. The preparation of a **White Paper on Genomic Medicine** in Catalonia.
2. The design and development of an **Integrated Plan on Genomic Medicine in Catalonia.**
3. The development of **pilot testing** that makes it possible to evaluate the efficacy of strategies based on genomic data.

Personalised Medicine Program

Genomic Medicine is also considered to be one of the strategic actions included in the Health Plan for Catalonia 2016-2020, with the respiratory tract as one of the priority areas. The Personalised Medicine Program is currently in the planning stage. Its principal objective is to generate a network that includes participation by hospitals, genomic analysis centres, data analysis platforms and university research centres.

This network will define the quality standards, the processes and the coding systems and will allow the implementation of a training program for practising physicians. This network of centres includes the National Centre for Genome Analysis and the Barcelona Supercomputing Centre.

This combination ensures that Catalonia's Personalised Medicine strategy will allow the development of proofs of concept and cost-effectiveness studies, which could be applicable throughout the healthcare system.

Genomes for Life Project (GCAT)

Project promoted by the Institute for Personalised and Predictive Cancer Medicine (IMPPC), the Germans Trias Institute and with the collaboration of the Blood and Tissue Bank and the Prevention Program of the ICO.

It was designed for the study of the genetic and environmental factors that lead to the appearance of chronic diseases in the general population.

Medbioinformatics

Project for translational research and Personalised Medicine in oncology and neuropsychiatry. This is a European consortium in which several Catalonian hospitals participate.

Andalusia.

Medical Genome Project

Precision Medicine is one of the priorities in the principal health and research strategies in Andalusia, including the Andalusia Genetics Plan, the Advanced Therapies Plan and the Andalusian Research, Development and Innovation Plan (PAIDI 2020).

Medical Genome Project (MGP)

A project that is addressing the sequencing of human genomes of patients and phenotyped control individuals.

The project is developed by the Department of Healthcare of the Regional Government of Andalusia, with the support of the Ministry of Science and Innovation.

It is located in the Science and Technology Park Cartuja in Seville and its purpose is to study, determine and classify a large number of genetically-based diseases, mainly those that are caused by a single gene (monogenic) and most of which are rare diseases. The genomes of healthy individuals have been sequenced until a single pattern was determined, a template that will make it possible, when compared in specific cases, to detect the anomalies that produce certain pathologies.

Twenty professionals from the fields of genetics, genomics and bio-computing are carrying out the work on this project, which is led by three researchers: professor Shomi Bhattacharya, associate scientific director of the Andalusian Research Program in Clinical Genetics and Genomic Medicine and currently director of the Andalusian Centre of Molecular Biology and Regenerative Medicine (CABIMER); professor Guillermo Antiñolo, director of the Andalusian Genetics Plan and director of the service of the Clinical Management Unit for Genetics, Reproduction and Foetal Medicine of the Virgen del Rocío University Hospital (Seville); and professor Joaquín Dopazo, head of the Bi-computing and Genomics Unit of the Príncipe Felipe Research Centre (Valencia) and associate scientific director for Bio-computing of the Genetics Plan of Andalusia.

It has a mega-sequencing platform and the data that is obtained is processed in a bio-computing platform with large computing and analysis capabilities.

The project is aimed at serving as a base for the implementation of Personalised Medicine in the Public Healthcare System of Andalusia. It is contributing information on quality and safety of the samples and allows constant updating of the associated information.

- Aimed at constructing a common non-pathological template for the entire human genome (healthy phenotype).
- Generate a standard map of the gene variations to be able to determine, in the initial phase, those that are involved in monogenic diseases (mostly rare diseases).
- In later phases, through the technological platform, polygenic diseases such as diabetes or hypertension, among others, will be addressed.
- Includes the participation of a team of professionals from the fields of genetics, genomics and bio-computing, working together with clinical researchers.

Source: http://www.juntadeandalucia.es/servicioandaluzdesalud/principal/documentosacc.asp?pagina=gr_actualidad1_b49

Other initiatives at the regional community level

Extremadura.

MEDEA Project. Applied Personalised Medicine

The objective of this project is the clinical implementation of Personalised Medicine in clinical research and Healthcare Services, to improve prescription of medication and increase the efficacy of Clinical Trials.

"Through the preliminary genetic analysis included in the healthcare card, the prescribing physician will be guided in the prescription process in order to optimise efficacy and reduce risks". The project will make it possible to develop the incorporation of patient genotypes into their health records, so that the prescriber can make a more informed decision when prescribing a particular medication.

Valencia Region

Strategy for the future of the Healthcare System

The Department of Universal Healthcare and Public Health has expressed the commitment to apply Precision Medicine as one of the fundamental strategies for the future of the Valencian healthcare system. In this line, the Department is focusing its efforts on investment in R&D in Precision Medicine, to produce omic data, as well as to generate the databases that combine this data with imaging data and information from direct consultation of patients and also for its complex storage and interpretation, so we expect significant progress in this area.

Future Clinic

The **FUTURE CLINIC** project is an initiative promoted by the public healthcare system aimed at developing tools to carry out the implementation of Personalised Medicine. The objective is to make the Region of Valencia a pioneer in the implementation of personalised diagnosis and treatment of cancer. The project is promoted by the Department of Healthcare, with the participation of the Principe Felipe Research Centre and the Polytechnic University of Valencia, as well as other companies and research entities in Valencia.

The following specific objectives have been proposed to achieve the general goal: research in the development of algorithms and genomic information processing systems; research on technologies and systems required to integrate this information into existing healthcare systems and research on technologies and solutions to assist with diagnosis that allow this genomic information to be incorporated into clinical practice.

Personalised Precision Medicine in RIS3 Strategies

In addition to the initiatives highlighted above, different Regions are promoting specific lines of research on Personalised Precision Medicine in the frameworks of their RIS3 smart specialisation strategies.

Consideration of Personalised Precision Medicine in regional research and innovation strategies for smart specialisation RIS3.

Regions	RIS3 Strategies Personalised Precision Medicine
Andalusia	Andalusia's Innovation Strategy 2020, RIS3 Andalusia. An important pathway for innovation in the health sector that must be incorporated into new developments of innovative products/services.
Balearic Islands	Innovation Strategy for smart specialisation of the Balearic Islands. Part of the Technologies for the Industry of health and well-being tourism, in the biotech sector.
Galicia	Código 100 is an Innovation Plan focused on aging. It includes an area of new therapies, the objectives of which include increased personalisation of care practices through the adoption of personalised treatments, in many cases associated with new diagnostic technologies. Promotion of public-private collaboration tools, such as the public pre-commercial purchase (CPP) and public purchase of innovative technology (CPTI).
Extremadura	Regional Strategy for Research and Innovation for smart specialisation in Extremadura, 2014-2020. Considers Precision Medicine to be a priority in health (genetics, pharmacogenomics, pharmacovigilance, omic technologies for the diagnosis and treatment of diseases.
Castile and Leon	Regional Strategy for Research and Innovation for smart specialisation, RIS3 2014-2020. Considered to be an area of action within cancer research and new diagnostic and therapeutic solutions and in biomedical research on priority problems.
Region of Madrid	Regional Strategy for Research and Innovation for smart specialisation of the Region of Madrid. Considers the support for research and innovation in Precision Medicine to be one of the 10 measures to be implemented. Considers the implementation and development of a Precision Medicine unit, which will make it possible to identify the most suitable treatments for each patient, based on their biological characteristics.
Basque Country	Strategy for RIS3 smart specialisation Euskadi. Considers Precision Medicine to be a priority area, including regenerative medicine for personalised treatment of diseases, according to the consideration of Personalised Medicine adopted in H2020.
Valencia Region	Smart Specialisation Strategy for Research and Innovation in the Valencia Region, RIS3-CV. Considered an action to be carried out as part of the innovation program in the area of healthcare and the policy for diversification and modernisation based on R&I.

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SEOM Sociedad Española de Oncología Médica

Sociedad Española de Neonatología SENeo

SEHH Sociedad Española de Hematología y Hemoterapia

Sociedad Española de Farmacología Clínica

Asociación Española de Pediatría AEP

AEGH Asociación Española de Genética Humana www.aegh.org

ATSEFFGC

sefh Sociedad Española de Farmacia Hospitalaria

Sociedad Española de Ginecología y Obstetricia S.E.G.O.

SEAP-IAP [Sociedad Española de Anatomía Patológica] [International Academy of Pathology]